

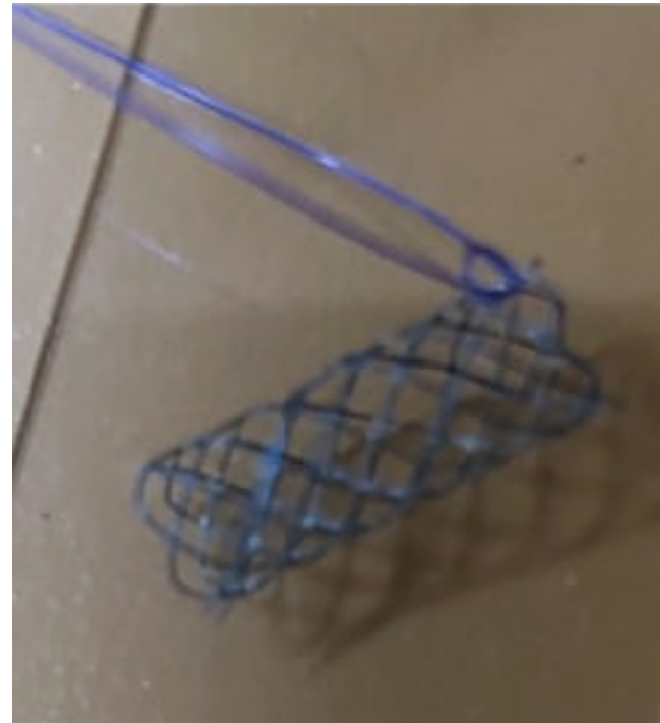
# Development of Double-Controlled Drug Eluting Stents with Nanotechnology

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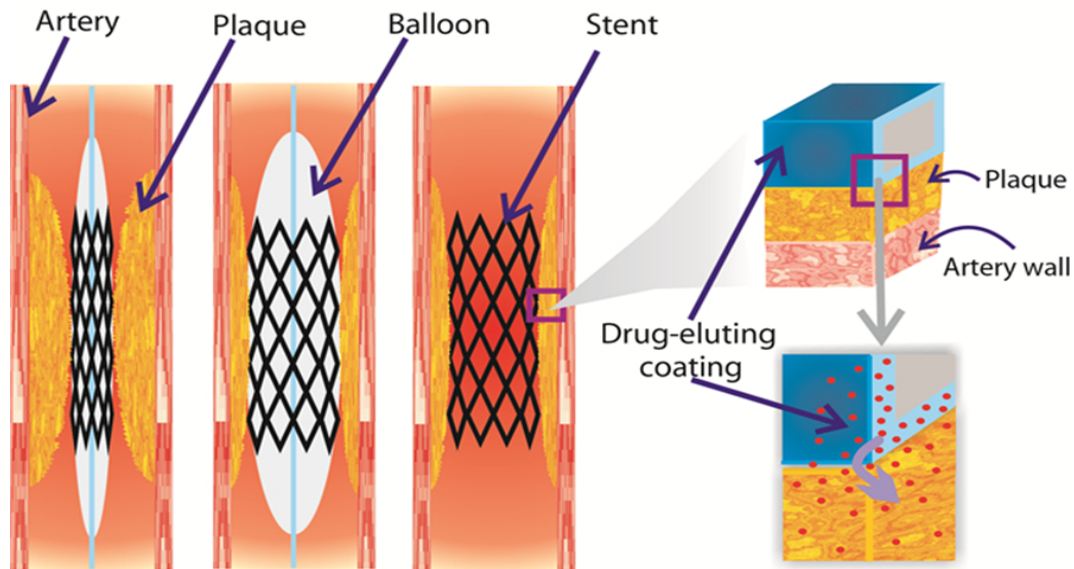
# Stent Project

## Description

- Used for drug delivering
- Consists of three parts
  - Stent platform
  - A polymer coating that binds the drug to the stent and releases the drug
  - Drug



# Drug-Eluting Stent (DES)



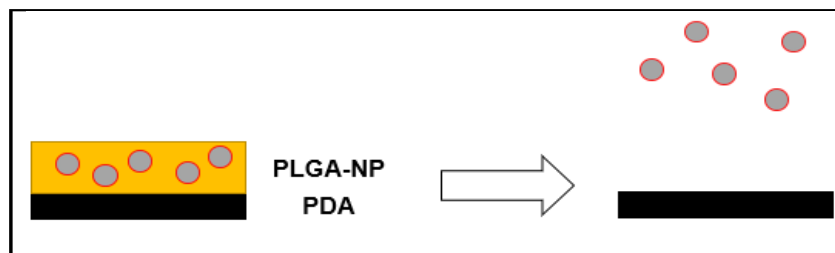
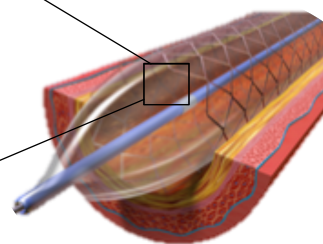
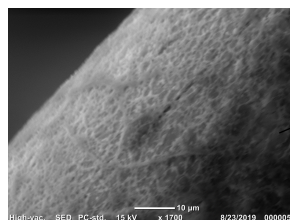
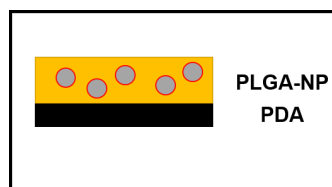
- Coated with medication that is slowly released to help prevent the growth of scar tissue in the artery lining
- Reduces the need for repeat angioplasty procedures
- Drug-eluting stents are more likely to keep the blockage from the recurring compared to bare metal stents
- Although DES was proved to be a safe and effective method in treatment of coronary artery stenosis by real world practices, there are still ongoing trials under evaluation for other subsets

# Purpose

The aim for this research is to use a non-vascular stent that encapsulates gemcitabine-loaded mesoporous silica nanoparticles (gMSNP) in polydopamine (PDA) and poly(lactic-co-glycolic) acid (PLGA) polymer matrix to advance the outcomes of drug release.

# Methodology

# Schematic



# PDA Coating

1. Dopamine hydrochloride was dissolved in 5mM Tris buffer (pH 8.5) to form 1 mg/mL solution
2. Stent was immersed
3. Dopamine polymerization onto stent
4. Washed with water
5. Repeat 1-4 two additional times in same condition

# PLGA Polymer Matrix Coating + Silica Nanoparticles (NP)

1. PLGA was dissolved in acetone
2. The PDA-coated stent was immersed in the PLGA solution and dried under room temperature
3. Repeat 1 and 2 two additional times in the same condition
4. Silica Nanoparticles were dispersed within the PLGA solution and coated onto the PDA-coated stent in the same manner



# Drug Release Data

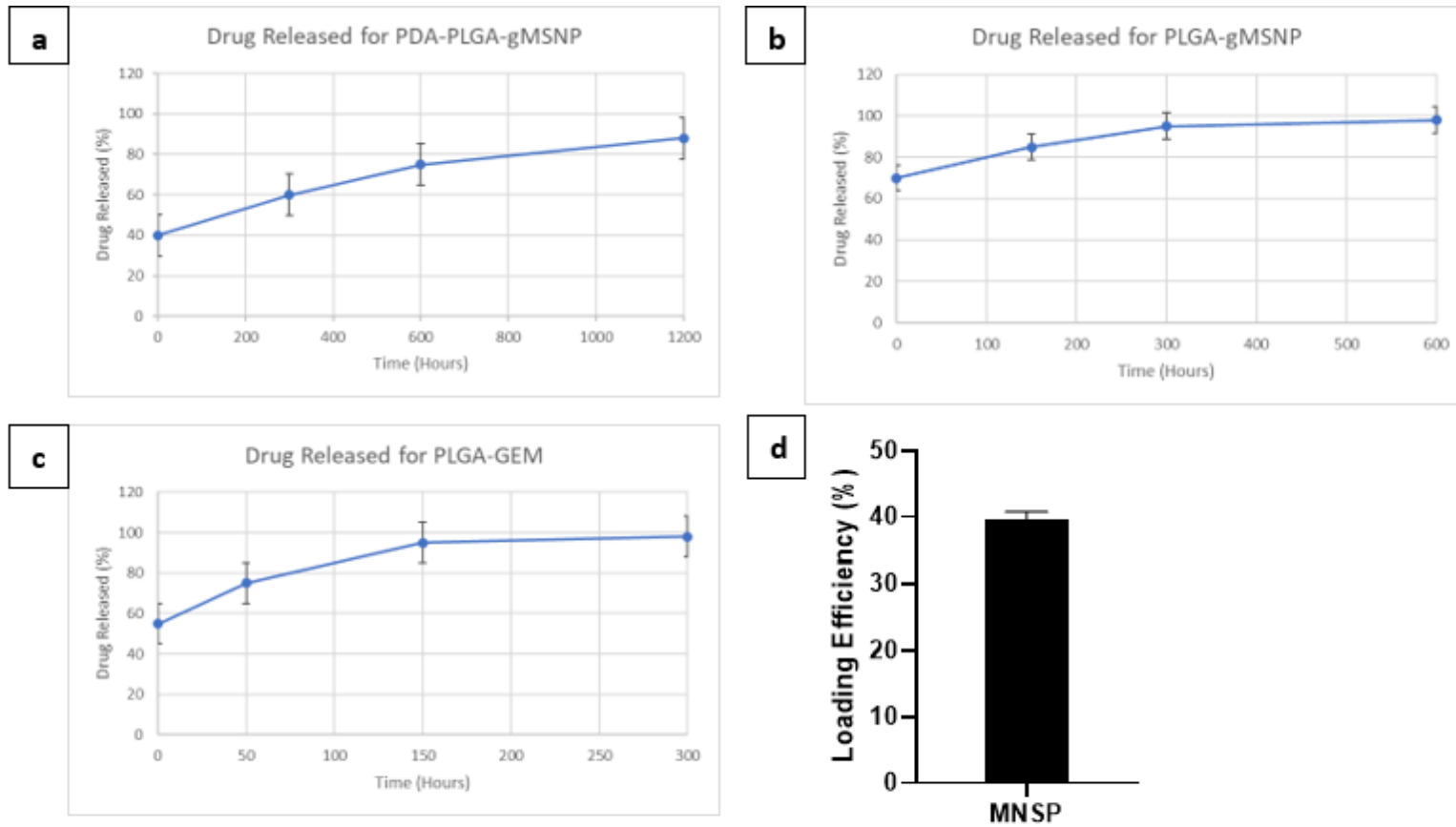


Figure. (a) Drug release profile of gMSNP with PDA-PLGA. (b) Drug release profile of gMSNP with PLGA coating. (c) Drug release profile of GEM with PLGA coating. (d) Loading efficiency of gemcitabine onto MSNPs.

# Conclusion

The data for the drug release collected showed a smaller burst release followed by a near zero-order release for the DES, which shows a constant rate of drug release over time. At 2 weeks after the initial release, the DES had 40 percent less drug released than PLGA loaded with pure GEM precipitates ( $p < 0.05$ ). The measured sustained drug release will eventually reduce the rate of restenosis that can be induced by stents.

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# References

- Azarbal, F., Price, M. (2019). Newer-generation Metallic Stents: Design, Performance Characteristics, and Outcomes. *Intervent Cardiol Clin*, 8, 95-109. <https://doi.org/10.1016/j.iccl.2018.11.001>.
- Volenc, K., Pohl, I. (2016). The Challenges: Stent Materials from the Perspective of the Manufacturer. *Gastrointestinal Intervention*, 5(2), 98-104. <https://doi.org/10.18528/gii160008>.
- Ong, A., McFadden, E., Regar, E., Jaegere, P., et al. (2005). Late Angiographic Stent Thrombosis (LAST) Events with Drug-Eluting Stents. *Journal of the American College of Cardiology*, 45(12), 2088-2092. <https://doi.org/10.1016/j.jacc.2005.02.086>.
- Lee, C., Lim, J., Low, A., Tan, H., Lim, Y. (2006). Late Angiographic Stent Thrombosis of Polymer Based Paclitaxel Eluting Stent. *Heart*, 92(4), 551-553. <https://doi.org/10.1136/hrt.2005.073619>.
- Byrne, R., Joner, M., Kastrati, A. (2015). Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Grüntzig Lecture ESC 2014. *European Heart Journal*, 36(47), 3320-3331. <https://doi.org/10.1093/eurheartj/ehv511>.
- Moses, J., Leon, M., Popma, J., Fitzgerald, P., et al. (2003). Sirolimus-Eluting Stents versus Standard Stents in Patients with Stenosis in a Native Coronary Artery. *The New England Journal of Medicine*, 349(14), 1315-23. <https://doi.org/10.1056/NEJMoa035071>.
- Lih, E., Kum, C., Park, W., Chun, S., et al. (2018). Modified Magnesium Hydroxide Nanoparticles Inhibit the Inflammatory Response to Biodegradable Poly(lactide-co-glycolide) Implant. *ACS Nano*, 12, 6917-25. <https://doi.org/10.1021/acsnano.8b02365>.

# References

- Chen, M., Liang, H., Chiu, Y., Chang, Y., Wei, H., Sung, H. (2005). A Novel Drug-eluting Stent Spray-coated with Multi-layers of Collagen and Sirolimus. *Journal of Controlled Release*, 108(1), 178-189. <https://doi.org/10.1016/j.jconrel.2005.07.022>.
- Fattori, R., Piva, T. (2003). Drug-eluting Stents in Vascular Intervention. *The Lancet*, 361(9353), 247-249. [https://doi.org/10.1016/S0140-6736\(03\)12275-1](https://doi.org/10.1016/S0140-6736(03)12275-1).
- Han, F., Thurecht, K., Whittaker, A., Smith, M. (2016). Bioerodable PLGA-Based Microparticles for Producing Sustained-Release Drug Formulations and Strategies for Improving Drug Loading. *Frontiers in Pharmacology*, 7, 185. <https://doi.org/10.3389/fphar.2016.00185>.
- Varde, N., Pack, D. (2004). Microspheres for controlled release drug delivery. *Expert Opinion on Biological Therapy*, 4(1), 35–51. <https://doi.org/10.1517/14712598.4.1.35>.
- Arias, L., Pessan, J., Vieira, A., Lima, T., Delbem, A., Monteiro, D. (2018). Iron Oxide Nanoparticles for Biomedical Applications: A Perspective on Synthesis, Drugs, Antimicrobial Activity, and Toxicity. *Antibiotics*, 7(2), 46. <https://doi.org/10.3390/antibiotics7020046>.
- Wang, X., Venkatraman, S., Boey, F., Loo, J., Tan, L. (2006). Controlled Release of Sirolimus From a Multilayered PLGA Stent Matrix. *Biomaterials*, 27(32), 5588-95. <https://doi.org/10.1016/j.biomaterials.2006.07.016>.
- Loo, J., Ooi, C., Boey, F. (2005). Degradation of Poly(lactide-co-glycolide) (PLGA) and Poly(l-lactide) (PLLA) by Electron Beam Radiation. *Biomaterials*, 26(12), 1359-1367. <https://doi.org/10.1016/j.biomaterials.2004.05.001>.

# References

- Loo, J., Ooi, C., Boey, F. (2005). Influence of electron-beam radiation on the hydrolytic degradation behaviour of poly(lactide-co-glycolide) (PLGA). *Biomaterials*, 26(18), 3809-3817. <https://doi.org/10.1016/j.biomaterials.2004.10.014>.
- Loo, J., Ooi, C., Wee, E., Boey, F. (2005). Effect of Isothermal Annealing on the Hydrolytic Degradation Rate of Poly(lactide-co-glycolide) (PLGA). *Biomaterials*, 26(16), 2827-2833. <https://doi.org/10.1016/j.biomaterials.2004.08.031>.
- Loo, J., Ooi, C., Tan, M., Boey, F. (2005). Isothermal Annealing of Poly(lactide-co-glycolide) (PLGA) and its Effect on Radiation Degradation. *Polymer International*, 54(4), 636-643. <https://doi.org/10.1002/pi.1724>.
- Loo, J., Ooi, C., Boey, F. (2004). Radiation Effects on Poly(lactide-co-glycolide) (PLGA) and Poly(L-lactide) (PLLA). *Polymer Degradation and Stability*, 83(2), 259-265. [https://doi.org/10.1016/S0141-3910\(03\)002714](https://doi.org/10.1016/S0141-3910(03)002714).
- Aguilar, L., Tumurbaatar, B., Ghavaminejad, A., Park, C., Kim, C. (2017). Functionalized Non-vascular Nitinol Stent via Electropolymerized Polydopamine Thin Film Coating Loaded with Bortezomib Adjunct to Hyperthermia Therapy. *Scientific Reports*, 7(9432), 1-11. <https://doi.org/10.1038/s41598-017-08833-x>.
- Liu, Y., Ai, K., Lu, L. (2014). Polydopamine and Its Derivative Materials: Synthesis and Promising Applications in Energy, Environmental, and Biomedical Fields. *Chemical Reviews*, 114(9), 5057-5115. <https://doi.org/10.1021/cr400407a>.